REMARKS

This responds to the Office Action mailed on February 19, 2008.

Claims 37 and 38 are added. Thus, claims 2, 4, 8-10, 24-37 and 38 are now pending in the application.

New claims 37 and 38 are directed to a method like those of claims 1 and 24.

In new claim 37, the antigenic peptide and the photosensitizing agent are administered to a patient and a viable cell presents the antigenic peptide on its surface, resulting in stimulation of an immune response. Support for administration of the antigenic peptide and the photosensitizing agent to a patient can be found throughout the specification as filed, for example, at page 25, line 25 to page 14, line 12, as well as in claims 1 and 24.

New claim 38 is drawn to a method of presenting an antigenic peptide or a part thereof on the surface of a viable antigen presenting cell, for example, to generate a population of antigen presenting cells as taught by the specification at page 13, lines 6-25. While claim 38 does not explicitly state that such a cell population is administered to a patient, the specification clearly teaches that this would be one use for the cells. Support for the method of claim 38 can be found throughout the specification as filed, for example, at page 5, lines 22-37, page 13, lines 6-25, and in the Example, as well as in claims 1 and 24.

Claims 35 and 36 are amended to recite that the peptide is 15 to 75 amino acids in length. Support for peptides with 15 to 75 amino acids, can be found throughout the application and claims as originally filed, for example, at page 7, lines 22-23 and in Example 2.

Applicant submits that no new matter has been added to the application.

§112 Rejections of the Claims

The Examiner has made two rejections under 35 U.S.C. § 112, first paragraph, relating to enablement and written description, which are separately addressed below

Enablement

Claims 2, 4, 8-10, 24-33 and 34 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Specifically, the Examiner's allegations emphasize that the specification does not provide sufficient evidence to enable one of skill in the art to express a molecule on a cell surface and generate an immune response. Applicant provides the following response with respect to claims 2, 4, 8-10, 24-34, 37 and 38.

Applicants submit that the Examiner has ignored the evidence of record that clearly shows presentation of peptide antigens on the surface of cells subjected to the methods of the invention, and killing of those cells by cytotoxic T cells (one type of immune response).

In particular, Applicants have provided data explicitly showing that cell killing by cytotoxic T cells occurs only when the cytotoxic T cell recognizes a previously internalized antigenic peptide on the surface of a cancer cell (see Example 2). These data also demonstrate that methods of the invention achieve presentation of sufficient antigenic peptide to allow recognition and cytotoxic T cell mediated cell killing of the cancer cells that internalized and presented the peptide on their cell surface (FIG. 3).

Contrary to the Examiner's allegations, use of antigen presenting cells was not required for such a cytotoxic T cell response. Instead, FM3 melanoma cells clearly displayed the MART-1 peptide when treated as recited in Applicant's claims (see Example 2 and the numerous responses previously filed with the Patent Office). Moreover, sufficient MART-1 peptide must have been displayed on the cell surface by MHC class I proteins because the cancer cells were killed by cytotoxic T cells (FIG. 3) and, as the Examiner knows, MHC class II proteins are not necessarily found on cancer cells.

Applicant submits that the Examiner's insistence that only antigen presenting cells can be used in the method is a failure on the part of the Examiner to consider and address the explicit language of the claims in view of certain basic scientific concepts.

Here, claim 2 is drawn to methods involving cancer cells while claims 24 and 38 are drawn to methods involving antigen presenting cells. Claim 37 is drawn to methods

involving viable cells because the antigenic peptide and the photosensitizing agent are administered to a patient. Hence, even though only selected regions of the patient treated according to claim 37 will be exposed to light, the peptide will likely be presented on a variety of cell surfaces, including antigen presenting cells and other cells (e.g., cancer cells), as is taught by the specification (see, e.g., page 8, lines 31-34 and the Examples).

The Examiner states that in addition to antigen presentation, costimulation that can only be provided by B cells, macrophages or dendritic cells is required for the generation of an immune response (page 3 of the Office Action, citing Janeway & Travers, IMMUNOBIOLOGY (1994)). While Applicants do not necessarily agree with this statement, these cells are antigen presenting cells and, because claims 24-27, 33, 34 and 38 are drawn to methods that utilize antigen presenting cells, the Examiner should withdraw this rejection with respect to these claims.

Moreover, MHC proteins (especially MHC I proteins) are present on the surfaces of *all* cell types in the body, such MHC proteins can display essentially any type of foreign antigen, and cytotoxic T cells are able to eliminate *any cell type* displaying the foreign antigen so long as the MHC proteins display the antigen. See, James D. Watson et al., MOLECULAR BIOLOGY OF THE GENE, 4th ed., pages 88-81 (The Benjamin/Cummings Publishing Company, Inc. 1987; submitted in a Supplemental Information Disclosure Statement filed Oct. 13, 2006). The Janeway document cited by the Examiner confirms this fact (see, for example, Figure 7.1), by disclosing antigen presentation on infected cells and the development of cytotoxic T cell responses to those cells. If, as the Examiner appears to be asserting, the immune system could recognize only certain antigen presenting cells, viral infections could spread aggressively and even minor infections would kill huge numbers of people.

Applicant submits that the Examiner is improperly requiring actual reduction to practice of all embodiments falling within the scope of the claims. However, this standard goes well beyond the true enablement standard, which only requires that the skilled person make or use the invention from what is taught in the specification coupled with the skilled person's knowledge, without undue experimentation. See, *Hybritech, Inc.*

v. Monoclonal Antibodies, Inc., 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987).

In essence, the requirement for enablement leads to a two part question. First, does the description teach how to make and use the invention and, second, could this be achieved without undue burden.

Applicant reminds the Examiner that as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. §112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Failure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. 112. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1533, 3 USPQ2d 1737, 1743 (Fed. Cir.), *cert. denied*, 484 U.S. 954 (1987).

Thus, the Examiner's statement that "there are no claims pending limited to the scope of the example" is improper to the extent that he is requiring Applicants to limit the claims to the scope of the Examples. The Examiner cannot require Applicants to actually reduce every aspect of the invention to practice. *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987). The Court in *Gould v. Quigg* held that "The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it." 822 F.2d at 1078, 3 USPQ2d at 1304 (quoting *In re Chilowsky*, 229 F.2d 457, 461, 108 USPQ 321, 325 (CCPA 1956)).

Thus, the specification is not required to provide data which illustrates that the invention has been extensively tested and fully proven as claimed, for example, by providing comprehensive *in vivo* data relating to the generation of an *in vivo* immune response. Extrapolation from appropriate *in vitro* data is acceptable because Applicants have employed the best possible *in vitro* model that could be provided to illustrate feasibility of the method *in vivo*. While generation of an immune response *in vitro* may not be possible, the next best experimental model has been utilized successfully by Applicants, namely the use of primed cytotoxic T cells (CTL) to ascertain if such cells react with cells treated according to the invention. This should satisfy enablement

because 35 U.S.C. §112, first paragraph, does not require that every element necessary to make the invention work be described; rather, it requires a description of the claimed invention in terms that will simply enable one skilled in the art to make and use the invention. A patent need not teach, and preferably omits, what is known in the art. *Lindemann Maschinenfabrik v. American Hoist and Derrick*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). Where an element is referred to in a generic sense, and one skilled in the art would be aware of what specifically would be sufficient to perform the task of that element, the generic reference is an adequate indication to that person skilled in the art to make or use the invention. *Alco Standard Corp. v. Tennessee Valley Auth.*, 597 F.Supp. 133 (N.D. Tenn. 1984), *aff'd,* 808 F.2d 1490 (Fed. Cir. 1986).

To fully demonstrate that the application enables one of skill in the art to make and use the invention, Applicants first address whether the specification teaches how to perform the invention as claimed.

Pursuant to language of claim 2, for example, the skilled person is taught to contact the cancer cell with an antigenic peptide and a photosensitizing agent, to irradiate the cell but not kill the cell to achieve cell surface presentation which results in cytotoxic T cell mediated cell killing. All these steps are clearly taught by Applicants' specification. The only variables involve the peptide and photosensitizers to be used and how to irradiate the cells without cell death but achieve cell surface presentation. The specification at page 7, from line 3 describes how to select the antigen. Both the size (page 7, lines 20-23) and the identity (see page 8, from line 11) are described. Mechanisms for targeting the antigenic molecule and/or the photosensitizer are discussed from page 11, line 14. The type of photosensitizer to be used is discussed on page 12, from line 11. Details on how the method should be carried out are described on page 12, from line 35. Moreover, the specification indicates, for example, that light doses similar to those described in WO96/07432 can be employed (see page 12, line 8). That document teaches the effect of light doses on the efficacy of internalization, and the use of various photosensitizers and different cells in photochemical internalization methods. Methods of light irradiation are also described in the present application on page 14, from line 13. Methods of avoiding cell death are described from page 14, line 19. Thus the

specification clearly and specifically teaches all the steps of the claimed method and how this method may be put into practice.

The second question is whether the invention can be put into practice without undue burden. As is apparent from the experiments conducted in the Examples of the present specification, as well as in the teachings of WO96/07432, the photochemical internalization (PCI) method can be readily applied with various photosensitizers and molecules for internalization and the method can be varied to prevent cell death by modifying the level of irradiation alone. For example, Figure 3 of WO96/07432 shows the effects of PCI treatment alone (open circles) in which cell survival decreases as irradiation time increases. Note that the contents of WO96/07432 are incorporated by reference into the present application (see Applicant's specification at page 12, lines 7-9). Comparable effects were seen in other cells with other photosensitizers. Clearly the photosensitizer, its dose and irradiation timing can be readily employed as described or modified with predictable results.

The only question which would seem to remain is whether a suitable response would be achieved *in vivo*. The Examiner has commented that any method involving generation of cytotoxic T cells (CTLs) involves the generation of activated T cells from naive T cells. Such activation of T cells can readily occur in vivo if the patient is first exposed to the peptide antigen and/or if a population of antigen presenting cells that display an antigenic peptide are administered to a patient. However, it is not necessary to pre-treat a patient with such a peptide (or such cells) because Salgaller *et al.* (Cancer Research 56: 4749-57 (1996)) illustrates that primed CTLs pre-exist. Thus the method as claimed could readily be put into practice insofar as relevant CTLs to many peptides already exist. The only aspect that the skilled person would need to determine is what peptides to use to reflect pre-existing primed CTL. This would not constitute an undue burden. The specification teaches the selection of antigens for cancer treatment on page 8, from line 11. Antigens of interest could be tested, e.g. by the method of Salgaller *et al.* to determine if relevant corresponding CTLs existed. The Salgaller *et al.* method, which involves analyzing interferon (IFN) release by CTLs in response to various peptides, is an entirely routine and simple *in vitro* test that would not constitute an undue burden to

perform. This could be performed rapidly for many test antigens at the same time. Indeed Salgaller *et al* itself, which was available at the time of the invention, identifies at least some antigens which would be appropriate for use in the methods of the present invention, because relevant primed CTLs already exist to those antigens.

The Examiner alleges it is not clear how the Valmori *et al.* (J, Immunol. 160: 1750-58 (1998)) article supports the claimed invention and, separately, that the specification teaches that all manner of antigens may be used and does not teach how to select appropriate molecules. Valmori *et al.* was provided to illustrate that one could perform the method as claimed if it was believed that primed CTLs were required to perform the method, *i.e.* to illustrate that all the relevant "starting materials" were readily available or could be produced according to methods known in the art. Valmori *et al.* also discloses various melanoma-associated antigens that can be recognized by cytotoxic T cells from cancer patients, providing evidence that antigenic peptides useful in the practice of the invention were available at the time of filing.

The Examiner also maintains that factors not disclosed in the specification are critical to the functionality of the claimed method, such as the toxicity of photosensitizing agents and peptides. Again, the Examiner is ignoring the teachings of Applicant's specification and Applicants' previously filed responses, which fully address this issue. Toxicity which results from irradiation during the photochemical internalization method can easily be controlled by adjusting the irradiation dose and the photosensitizer dose as taught in Applicants' specification. Thus, for example, the specification at page 1, line 24 to page 3, line 37, cautions the reader about the toxicity associated with photodynamic therapy, providing numerous reference citations and illustrating that photodynamic therapy is a well-known procedure. Clearly, these teachings alert the skilled artisan that use of photoactive compounds in combination with light irradiation can be toxic. Thus, the Examiner's statement that "it is now disclosed that factors not disclosed in the specification are critical to the functionality of the claimed method" is blatantly false. Applicants request that the Examiner withdraw this statement.

Moreover, the specification clearly describes how to use the photosensitizing agents and light irradiation properly in the methods of the invention. For example, page

14 of the specification discloses that the potency of the photosensitizing agents, and their ability to disrupt membranes on irradiation should be taken into account (lines 9-14). Page 14 of the specification discloses that the light irradiation step should be appropriately selected so that it does not deleteriously affect the viability and functionality of the cells (lines 14-27). Moreover, the proportion of cells that should be maintained in a live state are provided on page 14, lines 28 to 33. The specification also teaches that when exposing cells to light care should be taken because some cells may receive more light than others (page 14, line 34 to page 15, line 18). Furthermore, on page 15 it is explicitly taught that the methods may be modified to regulate the proportion of surviving cells by selection of appropriate light dosages and photosensitivity agents (lines 19-23). Thus, contrary to the Examiner's assertions, the specification clearly teaches how toxicity, which may result from the photochemical internalization method, should be avoided.

With respect to the toxicity of the antigenic peptide to be employed in the methods, Applicants submit that the Examiner is setting the bar very low for the skilled person's capabilities if this objection is to be given any weight. In essence, the Examiner asserts that the skilled person would not realize whether he or she should select a toxic or non-toxic molecule. Clearly, if the skilled artisan is using the methods of the invention, which involve presentation of an antigenic peptide on the surface of a live cell, a non-toxic peptide should be employed. Otherwise, the toxicity of the toxic molecule would kill the cell and no surface presentation could occur. If the toxicity of a molecule is unknown, appropriate experiments would be conducted to ensure that toxicity was not a problem. Even a lay person would be appreciative of the need not to administer potentially toxic agents to patients. No one of even minimal training in the art could be sufficiently confused to utilize a toxic molecule for the purposes of cell surface presentation. If that skilled person wished to employ toxic molecules, he or she would clearly use the methods available in other references and procedures (e.g., those in WO96/07432). Because this issue is so simple, and even the most poorly trained artisan in the field already understands it, Applicant submits that certain matters go without saying and do not need to be explicitly stated. A patent need not teach, and preferably

omits, what is known in the art. *Lindemann Maschinenfabrik v. American Hoist and Derrick*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

The only instances in which toxic substances would be appropriate would be when a cytotoxic effect was desired. In the present case, in the context of the nature of the invention clearly a toxic molecule is not contemplated as the method is explicitly designed to achieve cell surface presentation. It would be illogical to use toxic molecules for this purpose as this would defeat the method's purpose – a dead cell cannot effectively present the antigenic peptide.

In summary, the need to select a non-toxic molecule to allow the method to be performed was so apparent to any lay or skilled person reading the specification that it does not need to be specified. This is not a problem only brought to light by the Inventor's Declaration. This is a problem so obvious that it did not need to be stated.

The above comments refer to the selection of the molecule to be internalized and ultimately presented on the cell surface which necessarily should not be toxic. Toxicity in the photochemical internalization method is a separate matter, which can be tolerated to some extent when cell death is desired, e.g. in treating cancer. Methods for controlling the extent of cell death are fully described in the specification as set forth above and in our previous submissions.

At the end of the Examiner's discussion of enablement issues (page 6 of the Official Action), he states that the specification fails to address the issue of down-regulation of MHC class I by some tumors. Applicant again submits that the Examiner is requiring exceedingly high levels of disclosure that are not, by law, required to satisfy the enablement requirement.

Cancer vaccines are known in the art. Such vaccines work because they stimulate CTL production, which leads to the CTLs attacking tumor cells bearing the vaccine peptides. However, CTLs can only recognize and destroy cancer cells presenting the antigenic peptide in the context of a class I MHC molecule. Thus it is evident from the emergence of cancer vaccines as useful therapeutic agents that even if some tumors might exhibit down-regulation of MHC class I molecules, this is not a universal phenomenon

and MHC class I expression on cancer cells is sufficiently prevalent such that cancer vaccine development is appropriate.

Moreover, it is evident from the enclosed articles by Salgaller *et al* and Valmori *et al* that tumor-reactive CTL can be generated. These documents are specifically concerned with the development of CTL that will target tumor cells. Such CTL would only be useful if those tumor cells are able to express antigens by the MHC class I mechanisms. For example in Figure 2 on page 4755 in Salgaller *et al*, the amount of lysis of a melanoma line 624.38 mel was analyzed (filled squares). Lysis was clearly achieved, thus demonstrating that appropriate MHC I expression was present to permit CTL targeting. Similarly, Figure 1 of Valmori *et al* on page 1752 shows that the Me melanoma cell lines all experienced cell lysis by CTL from tumour infiltrated lymph nodes. Thus, these cancer cells all express MHC class I sufficiently for antigen presentation and CTL recognition to occur. Example 2 further illustrates that cancer cells (in that case melanoma cells) adequately express MHC class I to allow presentation of MART-1 peptide and its recognition by CTLs.

Moreover, the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v. E.I. duPont de Nemous & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure non-enabling). A disclosure of a large number of operable embodiments and the identification of a single inoperative embodiment did not render a claim broader than the enabled scope because undue experimentation was not involved in determining those embodiments that were operable. *In re Angstadt*, 537 F.2d 498, 502-503, 190 USPQ 214, 218 (CCPA 1976). Here, one of skill in the art could readily ascertain which cancer cells down-regulate MHC I by observing whether or not those cells present the antigenic peptide on their cell surfaces and/or whether primed cytotoxic T cells kill cancer cells subjected to the methods of the invention. Accordingly, the issue relating to down-regulation of MHC I is moot.

Accordingly, withdrawal of this rejection of claims 2, 4, 8-10, 24-34, 37 and 38 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Written Description

Claims 35 and 36 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description of methods employing peptides of 8 to 75 amino acids.

Applicant submits that the specification clearly provides support for methods employing peptides of 8 to 75 amino acids in length. However, solely to expedite the prosecution of this application, the claims have been amended to refer to peptides of about 15 to 75 amino acids. Support for the subject matter of peptides of about 15 to 75 amino acids is explicitly disclosed in the specification at page 7, lines 22-23.

Accordingly, withdrawal of this rejection of claims 35 and 36 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

§102 Rejection of the Claims

Claims 2, 4, 6, 8-10, 24-33 and 34 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by PCT Application Publication No. WO96/07432 by Berg. The Examiner alleges that WO96/07432 inherently anticipates the invention.

The Examiner asserts that WO96/07432, discloses *in vivo* uses of photochemical internalization and that these methods can be used in conjunction with cancer cells (citing page 6 of WO96/07432).

However, this is not an accurate reading of the teaching of the document because WO96/07432 only discloses photochemical internalization of toxins into cancer cells (see the Examples and page 7, lines 11-18 of WO96/07432). Internalization of such toxins has an immediate and direct effect on the cancer cells - they die. Such dead cells are, accordingly, not capable of displaying any peptide antigens on their cell surfaces. Thus, WO96/07432 cannot explicitly or inherently anticipate Applicant's claims.

The Examiner alleges that WO96/07432 teaches the delivery of peptides which may be antigenic for use *in vivo* (page 6) and that essentially all cells described in the

document are cancer cells. Therefore, according to the Examiner, WO96/07432 discloses identical methods as claimed in the invention. In arriving at this conclusion, the Examiner is combining parts of the document which should not be read together and is thus not giving the passages of that document their correct context. As such, the novelty objection is improperly framed.

Applicant submits that there are only two types of disclosures in a specification. The specific examples and the general disclosure of what methods could be performed. The specific teachings of the WO96/07432 examples have been discussed previously. In all those cases, toxic molecules are introduced into the cells, killing the cells before cell surface presentation of antigen can occur. If the toxic molecules are not successfully introduced such that the cells survive, those molecules can not be presented on the cell surface as they have not been internalized. Hence, the specific teachings of WO96/07432 do not anticipate Applicant's claims because there is no presentation of a peptide on the surface of the cell, as is required by Applicants claims.

Moving on to the general disclosure in the description, which is the teaching on which the Examiner now relies, the document teaches only cancer treatment with toxic molecules, gene therapy and some *in vitro* methods (see page 7, line 4 to page 8, line 4). The gene therapy suggestion can be ignored since is concerns the transfer of genes and the claims in issue are limited to the transfer of peptides. *In vitro* methods are concerned with performing methods in culture. There is no teaching in WO96/07432 that photochemical internalization should or can be used in conjunction with CTLs and, because only toxic molecules are used with cancer cells, no CTL mediated cell killing or immune response can occur as required by Applicant's claims.

Thus only the first teaching is relevant. However, this teaching is clearly concerned with the use of toxins as exemplified in the Examples of the document. Page 7, lines 14-18 specifies that for cancer treatment the method described is advantageous because the specificity of the toxin is enhanced. Thus only the use of a toxin is contemplated when the method is applied to cancer treatment. This is in line with the specific examples described above. As mentioned above, use of toxins on cancer cells,

even if performed *in vivo* does not lead to a method of the invention as they kill the cell if internalized and thus will not allow cell surface presentation.

The Examiner attempts to broaden the teachings of the document by referring to WO96/07432 claim 2 and stating that this recital of various molecules for internalization would be applied to cancer cells. This is clearly not the case. Claim 2 is dependent on claim 1, which is not limited to cancer cells. Claim 2 recites a list of nine different molecules for internalization. Thus, the use of protein or peptides from the list in claim 2 with cancer cells is simply not taught. This specific embodiment of cancer cells plus antigenic peptides is a combination which is not taught in WO96/07432. Indeed, it is not even a combination which is obvious because the document is very clear on what molecules should be used for cancer treatment, namely toxic molecules, since the authors of that document had no idea that internalized molecules would be presented on the cell surface and thus be of use in directing an immune response against cancer cells. Thus the combination which the Examiner asserts is disclosed in WO96/07432 is not disclosed, and is also contraindicated because the document clearly teaches the use of toxic molecules for cancer treatment.

Thus, the WO96/07432 document fails to provide a specific novelty destructive disclosure of the combination of cancer cells and proteins or peptides which are antigenic which could be presented on the cell surface. Whilst it is inappropriate for the assessment of novelty to consider what the document suggests, since this moves into obviousness considerations, even then, if the suggestions made by the document were followed they would not provide methods falling within the scope of the claims. The advent of the present invention that involves the use of antigenic molecules for administration by PCI to cancer cells is clearly distinct from the prior art. Before this, the combination was simply not recognized or taught as being of utility. To allege otherwise takes the teaching of WO96/07432 out of context when it is quite clear how it is intended to treat cancer cells using PCI, namely by the internalization of toxic molecules.

Thus Applicant's methods, involving antigen presentation on the cell surface of cancer cells and generation of CTL responses (claim 2) or an immune response (claim 24) are not taught in the cited document and do not inherently occur in the methods of

that document. In all cases, cancer treatment by using the methods of WO96/07432 would lead to the cancer cells being killed by photodynamic therapy or by the internalized toxic molecule because the authors were not aware that an internalized molecule can be presented on the cell surface allowing a CTL response. Thus, the authors specifically selected toxic molecules for their immediate and direct effect on the viability of the cell. This is unlike in the present case where internalization of the antigenic peptide does not in itself affect the cell's viability.

Therefore no inherency issue exists. Because the prior art method uses different molecules for internalization a different end result was obtained. In the case of the prior art method, toxic molecules would be used resulting in cell death. No viable cells containing those molecules which could then present them on the cell surface to elicit CTL mediated cell death would remain. Thus a CTL response would not be possible - unlike in the claimed method in which antigenic peptides are used which are not toxic and which would lead to viable cells after internalization so that the cells could still present antigenic peptides and allow the development of a CTL response.

Accordingly, withdrawal of this rejection of claims 2, 4, 6, 8-10, 24-33 and 34 under 35 U.S.C. § 102(b), is respectfully requested.

Conclusion

Applicants respectfully submit that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicants' attorney at (516) 795-6820 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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